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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**PENN-0701**
Inventors:	**Alain H. Rook**
Serial No.:	**09/419,328**
Filing Date:	**October 15, 1999**
Examiner:	**J. Dong**
Group Art Unit:	**1646**
Title:	**Methods for Treatment of Cutaneous T-Cell Lymphoma**

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Dear Sir:

APPEAL BRIEF

Table of Contents

Appendix 1 - Amended Claims

Appendix 2 - Page 227 of Verbik et al. (1996)

Appendix 3 - Declaration of Alain Rook

I. Real Party of Interest

The real party of interest is the Trustees of the University of Pennsylvania., assignee of all rights, title and interest in the instant application.

II. Related Appeals and Interferences

There are no related appeals or interferences.

III. Status of Claims

This application claims the benefit of priority from Provisional U.S. Application No. 60/104,342, filed October 15, 1998, abandoned, which was assigned to the assignee of the present invention.

An Office Action was mailed on October 4, 2000 wherein claims 1 through 3 were rejected. Specifically, claim 3 was rejected under 35 U.S.C. 102(b) as being anticipated by Haku et al. (1997) Claims 1 and 3 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Rook et al. (1996) in view of Haku et al. (1997).

A response was filed December 22, 2000 wherein claim 3 was amended.

In an Office Action dated March 14, 2001, pending claims 1 through 3 were rejected. Specifically, claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Rook et al. (1997). Claim 3 was rejected under 35 U.S.C. 102(a) as being anticipated by Lee

et al. (1998). Claims 1 through 3 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Rook et al. (1996), in view of Verbik et al. (1996). Claim 3 also was rejected under 35 U.S.C. 103(a) as being unpatentable over Rook et al. (1996) and Verbik et al. (1996), and further in view of Osaki et al. (1998) and Rook et al. (1997).

A response was filed by Appellant on August 3, 2001 wherein claim 2 was canceled, claim 3 was amended, and new claim 4 was added.

In an Office Action dated October 22, 2001, the rejection of claims 1, 3 and 4 was made Final. Specifically, claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Rook et al. (1997). Claims 1 and 3 were rejected under 35 U.S.C. 103(a) as being unpatentable over Rook et al. (1996) in view of Verbik et al. (1996). Claim 3 was rejected under 35 U.S.C. 103(a) as being unpatentable over Rook et al. (1996) and Verbik et al. (1996) and further in view of Rook et al. (1997). Claim 4 was rejected under 35 U.S.C. 103(a) as being unpatentable over Rook et al. (1996).

A response to the Final Rejection was filed by Appellant on March 21, 2002, wherein claims 1, 3 and 4 were amended.

In an Advisory Action dated April 17, 2002, the final rejection of claims 1, 3 and 4 was maintained but the amendments to claims 1, 3 and 4 were not entered.

Accordingly, the rejection of claim 1 under 35 U.S.C. 102(b), the rejection of claims 1 and 3 under 35 U.S.C. 103(a), the rejection of claim 3 under 35 U.S.C. 103(a), and the rejection of claim 4 under 35 U.S.C. 103(a) are on appeal. A copy of pending claims 1, 3 and 4 is attached hereto as Appendix 1.

IV. Status of Amendments

The amendment of claim 1, 3 and 4 in the Office Action response dated March 21, 2002 were not entered by the Examiner.

V. Summary of the Invention

The claimed invention includes compositions and methods for treatment of advanced cutaneous T cell lymphoma in humans, where the compositions comprise interleukin-12 in a pharmaceutically acceptable carrier administered with an adjunct therapeutic agent that stimulates interferon-γ production. Several specific adjunct agents are specified including a retinoid, interleukin-18, interferon-α, or interferon-γ. The methods as claimed are methods for treating advanced cutaneous T cell lymphoma in humans comprising administering interleukin-12 either alone or in combination with an adjunct therapeutic agent which stimulates interferon-γ production.

The claimed compositions and methods of use of the composition both are clearly described in the specification as filed, in particular at pages 5-10.

VI. Issues

The issues on appeal include: 1) whether claim 1 is anticipated under 35 U.S.C. 102(b) by Rook et al. (1997); 2) whether claims 1 and 3 are unpatentable under 35 U.S.C. 103(a) over Rook et al. (1996) in view of Verbik et al. (1996); 3) whether claim 3 is unpatentable under 35 U.S.C. 103(a) over Rook et al. (1996) and Verbik et al. (1996) and further in view of Rook et al. (1997); and 4) whether claim 4 is unpatentable under 35 U.S.C. 103(a) over Rook et al. (1996).

VII. Grouping of Claims

Claim 1 stands alone on the issue of anticipation under 35 U.S.C. 102(b) by Rook et al. (1997). Claims 1 and 3 stand or fall together on the issue of obviousness under 35 U.S.C. 103(a) over Rook et al. (1996) in view of Verbik et al. (1996). Claim 3 stands alone on the issue of obviousness under 35 U.S.C. 103(a) over Rook et al. (1996) and Verbik et al. (1996) and further in view of Rook et al. (1997). Claim 4 stands alone on the issue of obviousness under 35 U.S.C. 103(a) over Rook et al. (1996).

VIII. Arguments

Issue: Whether claim 1 is anticipated in light of Rook et al. (1997)

1. Examiner's basis for rejection

The Examiner has rejected claim 1 under 35 U.S.C. § 102(b) as being anticipated by Rook et al. (1997). The Examiner suggests that this paper suggests the clinical application of IL-12 to treat human cutaneous T cell lymphoma and provides a reasonable expectation of success because such a clinical trial must have been approved by the FDA. The Examiner has also dismissed a declaration provided by the inventor and author of this reference (Dr. Alain Rook) as being ineffective to overcome this rejection for it fails to establish a reduction to practice of the invention prior to the effective date of the prior art reference.

2. Summary of cited prior art teachings

Rook et al. (1997) is a review of the literature that supported a role for marked defects in interleukin-12 (IL-12) production in the pathogenesis of cutaneous T cell lymphoma. The evidence discussed for the role of IL-12 led the authors to perform *in vitro* studies with IL-12 as well as interferon-γ, studies that demonstrated the ability of these agents to suppress malignant cell growth *in vitro*. Nowhere does this paper teach the successful and effective *in vivo* use of IL-12, either with or without interferon-

γ, to treat cutaneous T cell lymphoma in humans. There is only a single statement in this paper that indicates "these studies led to a phase I trial of IL-12 to treat CTCL". No actual data on such a trial are provided or discussed. Additionally, the paper fails to provide details of how such a trial would be conducted.

3. The cited art fails to anticipate the present invention of claim 1.

A general level of operability is required in a reference to establish a prima facie case of obviousness or anticipation. See MPEP 2121. In accordance with MPEP 2121.01, the test in determining that quantum of prior art disclosure which is necessary to declare an applicant's invention "not novel" or "anticipated" within section 102, is whether a reference contains an "enabling disclosure". *In re Hoeksema*, 399F.2d 269(CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. Rook et al. (1997) do not teach treatment in humans. It was not until after the publication at issue that the clinical efficacy of IL-12 in cutaneous T cell lymphoma patients was discovered. This fact was stipulated in a declaration by the inventor, Dr. Alain Rook (attached hereto as Appendix 3). Specifically, as stated at page 2, top paragraph, lines 3-9, although the 1997 paper states that clinical trials were underway, they were actually only in the

planning stages in 1997 at the time of publication of the prior art reference. At that time in 1997, and as specifically declared by Dr. Rook, "no patients had yet actually participated in the study." Therefore, contrary to the Examiner's suggestion, this declaration provides evidence that the clinical study had not been performed and that IL-12 had not yet been shown to be effective as a treatment for cutaneous T cell lymphoma.

Applicants also respectfully pointed out that the Examiner had overstated the importance of a Phase I clinical trial in terms of FDA approval as well as in terms of showing one of skill that a compound would have expected clinical efficacy. Phase I clinical trials are merely safety studies wherein an escalating dose of a candidate drug is given to humans, usually to healthy volunteers, but sometimes to patients with a disease. A Phase I clinical trial is not a study of efficacy of a drug, or the ability of a candidate compound to produce a pharmacological effect that has therapeutic potential. Therefore, a mere statement in a paper that a Phase I clinical study is underway is not evidence that the FDA has approved that drug for any purpose or that the FDA has any belief that the drug has efficacy for treatment of disease. When a Phase I clinical study is begun, FDA has merely agreed that the drug to be studied has been shown to be safe for use in humans, based on animal data. The FDA does not address efficacy of a drug until Phase II and III studies have been completed and submitted for

agency review in the form of a New Drug Application (NDA). Clearly, then, a statement in a paper that a Phase I trial is underway is not enabling for one of skill to understand that the drug being tested in the Phase I trial has efficacy to treat disease. In fact, doses administered in a Phase I study are not designed to prove efficacy, only safety. Accordingly, this paper by Rook et al. (1997) does not anticipate the instant invention of claim 1 which is drawn to treatment of advanced cutaneous T cell lymphoma. It is only with the specification in hand that describes results of treatment of humans that one of skill would see that the invention of claim 1 had been reduced to practice.

Therefore, based on the requirements of MPEP 2131, the paper by Rook et al. (1997) fails to anticipate the instant invention.

Issue: Whether claims 1 and 3 are obvious under 35 U.S.C. 103(a) over Rook et al. (1996) in view of Verbik et al. (1996)

1. Examiner's basis of rejection

The Examiner suggests that Rook et al. (1996) demonstrate that depressed interferon-γ production is normalized *in vitro*, indicating that a marked defect in IL-12 production by peripheral blood mononuclear cells in Sezary syndrome may be an important factor in the failure to produce normal amounts of interferon-γ and

mediating normal cell-mediated immunity. The Examiner acknowledges that Rook et al. (1996) do not teach a method of *in vivo* treatment but then asserts that Verbik et al. (1996) teaches a method of treatment of a murine lymphoma with IL-12 in mice, providing for a reasonable expectation of success in treating lymphoma in humans. The Examiner also suggests that the requirement of a reasonable expectation of success does not rest on a complete certainty of success and that virtually all clinical applications are based on *in vitro* and/or *in vivo* animal studies such as provided by Verbik et al. (1996).

2. Summary of the prior art teachings

Rook et al. (1996) is a paper by the inventor of the present application that describes early studies with IL-12 in cells. This paper describes *in vitro* cell culture experiments with peripheral blood mononuclear cells (PBMCs) and a single cytokine, IL-12. The results of the *in vitro* studies showed that their was a marked defect in IL-12 production in these cells in patients with Sezary syndrome and that depressed interferon-γ production in these cells can be normalized by contact of the cells with IL-12. This paper does not teach treatment of advanced cutaneous T cell lymphoma in humans using IL-12 either alone or in combination with agents that increase interferon-γ production as claimed in claims 1 and 3.

Verbik et al. (1996) teach the administration of IL-12 to mice suffering from liver lymphoma. Even as such, the use of IL-12 with other interleukins caused unexplained early deaths in the test mice. As is taught on page 227 of the reference (attached as Appendix 2), the IL-12 was believed to have induced secretion of interferon-γ causing gastrointestinal damage to the tissue of the mice and resulting in their death. Further, mice undergoing radiation after administration of IL-12 suffered severe gastrointestinal damage that was much more pronounced than damage induced by radiation alone (see page 227, column 2). Verbik et al. (1996) further teach that the mechanisms through which the IL-12 mediates *in vivo* anti-tumor responses is not fully understood. Therefore, even though early deaths occurred in groups of animals receiving combined treatments, the authors of this reference believed that it was IL-12 that was leading to unacceptable toxicity.

3. The combination of cited art fails to make obvious the present invention

To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a) three basic criteria mush be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine

reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all the claim limitations.

The cited combination of prior art references fails to meet all of these criteria with respect to the instant invention of claims 1 and 3. Neither of the cited prior art references provide one of skill in the art with a reasonable expectation of successfully treating advanced cutaneous T cell lymphoma in a human with administration of IL-12 alone or in combination with an adjunct therapeutic agent that stimulates interferon-γ production.

As acknowledged by the Examiner, Rook et al. (1996) do not teach a method of in vivo treatment using IL-12. Further, Rook et al. (1996) fail to teach administration of IL-12 even *in vitro* with an adjunct therapeutic agent as claimed in claim 3.

As discussed *supra*, Verbik et al. (1996) actually put into question the safe use of IL-12 by showing that there was unexpected toxicity in animals that they attributed to IL-12. Although cancer chemotherapy agents often have the potential for toxicity, it is the presence of these toxic effects that is usually a deciding factor when one of skill decides whether or not to test an agent in humans. The presence of life-threatening toxicity with treatment in animals often will lead one of skill to not test the compound in humans. The fact that Verbik et al. (1996) teach that early deaths resulted with use of IL-12 in animals, not just a minor toxic

effect but a life-threatening one, indicates that the use of IL-12 in conjunction with other therapeutics especially needs to be shown to be safe before testing in humans is begun. Therefore, the reference of Verbik et al. (1996) does not provide one of skill with a reasonable expectation of success for use of IL-12 in humans as an effective treatment for advanced cutaneous T cell lymphoma.

Accordingly, neither of the cited prior art references provide one of skill in the art with a reasonable expectation of successfully treating advanced cutaneous T cell lymphoma in a human via administration of IL-12 either alone or in combination with an adjunct therapeutic agent. In addition, there is no suggestion or teaching in the cited references to combine reference teachings as required. On the contrary, one of skill would refrain from administering IL-12 to humans based on the teachings of Verbik et al. (1996) and Rook et al. (1996) as combined by the Examiner. As a result, these references fail to establish a prima case of obviousness under 35 U.S.C. 103(a).

Issue: Whether claim 3 is obvious under 35 U.S.C. 103(a) in light of Rook et al. (1996) and Verbik et al. (1996) and further in view of Rook et al. (1997)

1. Examiner's basis of rejection

The Examiner suggests that Rook et al. (1996) demonstrate that depressed interferon-γ production is normalized *in vitro*, indicating that a marked defect in IL-12 production by PBMCs in Sezary syndrome may be an important factor in the failure to produce normal amounts of interferon-γ and mediating normal cell-mediated immunity. The Examiner acknowledges that Rook et al. (1996) do not teach a method of *in vivo* treatment but then asserts that Verbik et al. (1996) teaches a method of treatment of a murine lymphoma with IL-12 in mice, providing for a reasonable expectation of success in treating lymphoma in humans. The Examiner then suggests that it would have been obvious for one of skill to make a composition comprising a recombinant IL-12 and interferon-γ or a retinoid in order to practice the method of claim 3 because Rook et al. (1997) establish that IL-12 is being studied in a Phase I clinical trial.

2. Summary of the prior art teachings

Rook et al. (1996) is a paper by the inventor of the present application that describes early studies with IL-12 in cells. This paper describes *in vitro* cell culture experiments with peripheral blood mononuclear cells (PBMCs) and a single cytokine, IL-12. The results of the *in vitro* studies showed that their was a marked defect in IL-12 production in these cells in patients with Sezary

syndrome and that depressed interferon-γ production in these cells can be normalized by contact of the cells with IL-12. This paper does not teach treatment of advanced cutaneous T cell lymphoma in humans using IL-12 either alone or in combination with agents that increase interferon-γ production as claimed in claims 1 and 3.

Verbik et al. (1996) teach the administration of IL-12 to mice suffering from liver lymphoma. Even as such, the use of IL-12 with other interleukins caused unexplained early deaths in the test mice. As is taught on page 227 of the reference (attached as Appendix 2), the IL-12 was believed to have induced secretion of interferon-γ causing gastrointestinal damage to the tissue of the mice and resulting in their death. Further, mice undergoing radiation after administration of IL-12 suffered severe gastrointestinal damage that was much more pronounced than damage induced by radiation alone (see page 227, column 2). Verbik et al. (1996) further teach that the mechanisms through which the IL-12 mediates *in vivo* anti-tumor responses is not fully understood. Therefore, even though early deaths occurred in groups of animals receiving combined treatments, the authors of this reference believed that it was IL-12 that was leading to unacceptable toxicity.

Rook et al. (1997) is a review of the literature that supported a role for marked defects in interleukin-12 (IL-12) production in the pathogenesis of cutaneous T cell lymphoma. The

evidence discussed for the role of IL-12 led the authors to perform *in vitro* studies with IL-12 as well as interferon-γ, studies that demonstrated the ability of these agents to suppress malignant cell growth *in vitro*. Nowhere does this paper teach the successful and effective *in vivo* use of IL-12, either with or without interferon-γ, to treat cutaneous T cell lymphoma in humans. There is only a single statement in this paper that indicates "these studies led to a phase I trial of IL-12 to treat CTCL". No actual data on such a trial are provided or discussed. Additionally, the paper fails to provide details of how such a trial would be conducted.

3. The combination of cited art fails to make obvious the present invention

As discussed in detail *supra*, the combination of Rook et al. (1996) and Verbik et al. (1996) fails to provide one of skill with a teaching of the clinical use of IL-12 either alone or in combination with adjunct therapeutic agents for treatment of advanced cutaneous T cell lymphoma in humans. Further, as discussed *supra*, this combination of prior art fails to provide even a reasonable expectation of success in humans in teaching that IL-12 has life-threatening toxicity, a fact that would lead one of skill to question the safe use of IL-12 in humans.

Also as discussed *supra*, a general level of operability is required in a reference to establish a *prima facie* case of

obviousness or anticipation. See MPEP 2121. In accordance with MPEP 2121.01, the test in determining that quantum of prior art disclosure which is necessary to declare an applicant's invention obvious within section 103, is whether a reference contains an "enabling disclosure". *In re Hoeksema*, 399F.2d 269(CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. Rook et al. (1997) do not teach treatment in humans. It was not until after the publication at issue that the clinical efficacy of IL-12 in cutaneous T cell lymphoma patients was discovered. This fact was stipulated in a declaration by the inventor, Dr. Alain Rook (attached hereto as Appendix 3). Specifically, as stated at page 2, top paragraph, lines 3-9, although the 1997 paper states that clinical trials were underway, they were actually only in the planning stages in 1997 at the time of publication of the prior art reference. At that time in 1997, and as specifically declared by Dr. Rook, "no patients had yet actually participated in the study." Therefore, contrary to the Examiner's suggestion, this declaration provides evidence that the clinical study had not been performed and that IL-12 had not yet been shown to be effective as a treatment for cutaneous T cell lymphoma.

Applicants also respectfully pointed out that the Examiner had overstated the importance of a Phase I clinical trial in terms of FDA approval as well as in terms of showing one of skill that a

compound would have expected clinical efficacy. Phase I clinical trials are merely safety studies wherein an escalating dose of a candidate drug is given to humans, usually to healthy volunteers, but sometimes to patients with a disease. A Phase I clinical trial is not a study of efficacy of a drug, or the ability of a candidate compound to produce a pharmacological effect that has therapeutic potential. Therefore, a mere statement in a paper that a Phase I clinical study is underway is not evidence that the FDA has approved that drug for any purpose or that the FDA has any belief that the drug has efficacy for treatment of disease. When a Phase I clinical study is begun, FDA has merely agreed that the drug to be studied has been shown to be safe for use in humans, based on animal data. The FDA does not address efficacy of a drug until Phase II and III studies have been completed and submitted for agency review in the form of a New Drug Application (NDA). Clearly, then, a statement in a paper that a Phase I trial is underway is not enabling for one of skill to understand that the drug being tested in the Phase I trial has efficacy to treat disease. In fact, doses administered in a Phase I study are not designed to prove efficacy, only safety. Accordingly, this paper by Rook et al. (1997), when combined with the papers of Rook et al. 1996) and Verbik et al. (1996), does not make obvious the instant invention of claim 3 which is drawn to treatment of advanced cutaneous T cell lymphoma. It is only with the specification in

hand that describes results of treatment of humans that one of skill would see that the invention of claim 3 had been reduced to practice.

To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a) three basic criteria mush be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all the claim limitations.

The cited combination of prior art references fails to meet all of these criteria with respect to the instant invention of claim 3. None of the cited prior art references provide one of skill in the art with a reasonable expectation of successfully treating advanced cutaneous T cell lymphoma in a human with administration of IL-12 alone or in combination with an adjunct therapeutic agent that stimulates interferon-γ production.

As acknowledged by the Examiner, Rook et al. (1996) do not teach a method of *in vivo* treatment using IL-12. Further, Rook et al. (1996) fail to teach administration of IL-12 even *in vitro* with an adjunct therapeutic agent as claimed in claim 3. Verbik et al. (1996) actually put into question the safe use of IL-12 by showing that there was unexpected toxicity in animals that they attributed

to IL-12. Finally, Rook et al. (1997) do not teach use of IL-12 with adjunct therapeutic agents in a clinical trial, as stipulated by the declaration provided by the inventor (Appendix 3)

Therefore, based on the requirements of MPEP 2143, this combination of prior art fails to make obvious the instant invention of claim 3.

Issue: Whether claim 4 is obvious under 35 U.S.C. 103(a) in light of Rook et al. (1996).

1. Examiner's basis of rejection

The Examiner suggested that although Rook et al. (1996) do not teach a method of *in vivo* treatment, it would have been *prima facie* obvious for one of ordinary skill to design a method for treatment of cutaneous T cell lymphoma based on the teaching of Rook et al. (1996) and the suggestions that Sezary syndrome, an advanced form of lymphoma, is characterized by marked depression of interferon-γ production and a defect in IL-12 production by PBMCs. Further, the Examiner suggested that one of skill would have been motivated to treat cutaneous T cell lymphoma by administering IL-12 with an adjunct agent that stimulates interferon-γ production at Rook's suggestion and would have reasonably expected success because such combinations would correct both defects in these patients. The Examiner acknowledges that the reference is silent about a

pharmaceutically acceptable carrier but that this is well known in the art.

2. Summary of the prior art teaching

Rook et al. (1996) is a paper by the inventor of the present application that describes early studies with IL-12 in cells. This paper describes *in vitro* cell culture experiments with peripheral blood mononuclear cells (PBMCs) and a single cytokine, IL-12. The results of the *in vitro* studies showed that their was a marked defect in IL-12 production in these cells in patients with Sezary syndrome and that depressed interferon-γ production in these cells can be normalized by contact of the cells with IL-12. This paper does not teach treatment of advanced cutaneous T cell lymphoma in humans using IL-12 in combination with agents that increase interferon-γ production as claimed in claim 4.

3. The combination of cited art fails to make obvious the present invention

To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a) three basic criteria mush be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable

expectation of success. Finally, the prior art must teach or suggest all the claim limitations.

The cited combination of prior art references fails to meet all of these criteria with respect to the instant invention of claim 4. None of the cited prior art references provide one of skill in the art with a reasonable expectation of successfully treating advanced cutaneous T cell lymphoma in a human with administration of IL-12 in combination with an adjunct therapeutic agent that stimulates interferon-γ production.

As discussed *supra*, Rook et al. (1996) teach only *in vitro* culture experiments with PBMCs and a single cytokine, IL-12. Rook et al. (1996) do not teach a composition comprising recombinant IL-12 with a separate adjunct agent that stimulates production of interferon-γ, as is disclosed and claimed in the instant invention of claim 4. Further, MPEP 2143 and the Courts are quite clear; both the teaching and suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure. In *re Vacek*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The cited prior art fails to provide this reasonable expectation of success. It is only with the instant specification in hand, which demonstrates the efficacy of Applicant's invention that one of skill has a reasonable expectation of success. Accordingly, the cited prior

art fails to establish a *prima facie* case of obviousness as set forth in MPEP 2143.

IX. Conclusion

The references cited by the Examiner clearly do not provide the requisite teaching to anticipate the instant invention and also fail to provide either a teaching or suggestion to render the claimed invention obvious.

Respectfully submitted,

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Date: **June 19, 2002**

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TRANSMITTAL LETTER (General - Patent Pending)	Docket No. PENN-0701

In Re Application Of: Alain H. Rook

Serial No.	Filing Date	Examiner	Group Art Unit
09/419,328	October 15, 1999	D. Jiang	1646

Title: METHODS FOR TREATMENT OF CUTANEOUS T-CELL LYMPHOMA

TO THE ASSISTANT COMMISSIONER FOR PATENTS:

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Jane Massey Licata
Signature

Dated: **June 19, 2002**

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1) General Transmittal Letter (in triplicate);

2) Appeal Brief (in triplicate);

3) Return Post Card; and

4) Authorization to charge deposit account for $160.00.

Jane Massey Licata

JANE MASSEY LICATA